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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/664,444	09/18/2000	John C Bell	18003	4773

7590 07/12/2002

Lewis J Kreisler
Legal Department
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EXAMINER	
ZEMAN, ROBERT A	

ART UNIT	PAPER NUMBER
1645	18

DATE MAILED: 07/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/664,444	Applicant(s) BELL ET AL.	
	Examiner Robert A Zeman	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) *2-4,14-17 and 38-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-13 and 18-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-63* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5-7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II in Paper No. 17 is acknowledged. The traversal is on the ground(s) that there would not be a serious burden on the Examiner to search all groups together. This is not found persuasive because the searches of the various groups would not be coextensive in scope.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-63 are pending. Claims 2-4, 14-17 and 38-63 are withdrawn for consideration as they are drawn to a nonelected invention. Claims 1, 5-13 and 18-37 are currently under examination.

Information Disclosure Statement

The various Information Disclosure Statements (Paper Nos. 5-8) are acknowledged. Initialed copies are contained herein. However, not all the cited references were available and consequently were not considered. Said references will be considered when said references become available.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Claim Objections

Claim1, 5-13 and 18-34 are objected to because of the following informalities: Claim 1 recites nonelected inventions. Appropriate correction is required.

The instant claims are drawn to methods of reducing the viability of hematopoietic tumor cells by administering a virus and optionally interferon.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-13 and 18-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods utilizing **VSV** for reducing the viability of mylogenous leukemia cell lines *in vitro*, does not reasonably provide enablement for the utilization of **all** viruses (that are not common human pathogens) for the reduction of viability of all hematopoietic tumor cells (either *in vivo* or *in vitro)*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. To use the invention as claimed one must be able to differentially infect a susceptible tumor cell resulting in a reduction in said cell's viability. While the specification provides great detail on the susceptibility of different cell types to VSV and the protective effect of alpha interferon against VSV infection, the specification is silent on the what viruses other than VSV would induce the claimed antitumor effect. The

specification is equally silent on which interferons other than alpha interferon would provide normal cells protection from viral infection. Additionally, the instant claims are drawn to **all** forms of hematopoietic tumor cells, while the specification has demonstrated only two leukemia cell lines (MD7E and L1210), a couple of AML cell lines OCI/AML3 and AML5, one CML cell line (K-562) and a T-cell leukemia (MOLT-4) that are that are susceptible to VSV infection. VSV was shown to reduce the viability of only the AML, CML and T-cell leukemia cell lines. The specification is silent on what receptor is utilized by VSV for cell entry. The specification is equally silent on what tumor cell types are killed by VSV infection. The invention is predicated on the susceptible tumor cells lacking PKR activity, but the specification is silent on which hematopoietic tumor cells lack said function. Claims 32-34 are drawn to the *in vivo* application of the claimed methods. People of skill in the art require documented evidence that a benefit can be derived by the therapeutic application of a given substance; however, a survey of the relevant art does not indicate that substances such as those claimed provide such benefit. The instant specification fails to provide direction on which viruses, if any, are capable of eliciting a therapeutic response (tumor cell death). Moreover, the specification is equally silent on how said viruses are to be administered to said subject.

While the specification teaches how to use VSV to reduce the viability of melanoma cells (*in vivo*) and provides *in vitro* data showing effects of VSV infection on several hematopoietic cell lines (either with or without alpha interferon), it does not provide any basis for correlating the *in vitro* results with beneficial effects that could reasonably be expected when said viruses are administered *in vivo* to "treat" hematopoietic tumor cells, although *in vivo* use is clearly encompassed by the claims. Lacking either direct evidence for *in vivo* benefit, or a reasonable

basis for correlating *in vitro* data as exemplified with *in vivo* benefit, the specification cannot be said to teach how to use the claimed viruses as pharmaceuticals.

Claims 1, 5-13 and 18-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the use of the phrase "common human pathogen". While the specification defines said term as "a virus that is found mostly in non-human hosts" and "viruses that are not typically found in the general human population", it is unclear what the metes and bounds of the claimed invention. VSV infection is a common problem with farmers and other people who come in contact with soil (Fields Virology 3rd Edition, page 1140). Said infections result in the formation of dermal blisters (vesicles). Consequently, VSV would be classified as a "common human pathogen" which contrary to the instant claims and the instant specification.

Claim 1 is rendered vague and indefinite by the use of the term "administering to the tumor cell a virus". It is unclear what is meant by said term. Is said virus "injected" into said tumor cell or merely introduced into said cells environment?

Claim 18 is rendered vague and indefinite by the use of the term "substantially no PKR activity". It is unclear what is meant by said term. At what level does PKR activity become "substantially no" PKR activity?

Claim 24 is rendered vague and indefinite by the use of the term "administering interferon to the tumor cell". It is unclear what is meant by said term. Is said virus "injected" into said tumor cell or merely introduced into said cells environment?

Claim 34 recites improper Markush language. The ultimate member of the group should be preceded by "and".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5-7 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by McCormick (U.S. Patent 5,677,178 – IDS-7).

The instant claims are drawn to methods of reducing the viability of hematopoietic tumor cells by administering a virus that is not a common human pathogen.

McCormick et al. disclose methods utilizing genetically reengineered adenoviruses to treat neoplasms (see abstract). McCormick further discloses "lymphocytic leukemias may be treated by administering an effective antineoplastic dosage of an appropriate replication deficient adenovirus" (see column 16, lines 62-64). Since lymphocytic leukemias are classified as hematopoietic cancers and since the recombinant adenoviruses disclosed are not common human pathogens, McCormick anticipates all the limitations of the instant claims.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A Zeman whose telephone number is (703) 308-7991. The examiner can normally be reached on M-Th 7:30 am - 5:00 pm and Alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Donna Wortman can be reached on (703) 308-1032. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DONNA WORTMAN
PRIMARY EXAMINER

Robert A. Zeman
July 11, 2002